# AMITROLE CAS No. 61-82-5

First Listed in the Second Annual Report on Carcinogens

#### **CARCINOGENICITY**

Amitrole is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity of amitrole in experimental animals (IARC V.7, 1974; IARC S.4, 1982; IARC V.41, 1986; IARC S.7, 1987). When administered in the diet, amitrole increased the incidence of hepatocellular carcinomas and adenomas in mice of both sexes. When administered by gavage to weanling mice of both sexes followed by dietary administration, amitrole induced tumors of the thyroid and increased the incidence of tumors of the liver. When mice of both sexes were nursed by dams fed diets containing amitrole, the incidence of hepatocellular carcinomas and adenomas was increased in male but not female animals. When administered topically, amitrole did not induce skin tumors in mice of both sexes. One study of transplacental exposure to amitrole by mice yielded inconclusive results. When administered in the diet, amitrole induced malignant and benign tumors of the thyroid in rats of both sexes and benign pituitary tumors in female rats. When administered in the drinking water, amitrole induced follicular cell carcinomas of the thyroid in female rats. When administered in the diet, no carcinogenic effect was observed in hamsters of both sexes.

There are no adequate data available to evaluate the carcinogenicity of amitrole in humans. In a small cohort study of Swedish railroad workers who had sprayed herbicides, there was a statistically significant excess of all cancers among those exposed to both amitrole and chlorophenoxy herbicides, but not among those exposed mainly to amitrole (IARC V.7, 1974; IARC S.4, 1982; IARC V.41, 1986; IARC S.7, 1987).

## **PROPERTIES**

Amitrole occurs as colorless crystals. It is insoluble in ether, acetone and hydrocarbons; slightly soluble in chloroform, methylene chloride, acetonitrile, and ethyl acetate; and soluble in water and ethanol. Amitrole is formulated into soluble powders, liquids, and aerosols and is available in the United States as a technical grade containing 90% minimum active ingredient. When heated to decomposition, it emits toxic fumes of nitrogen oxides ( $NO_x$ ).

#### **USE**

Amitrole was first patented for use in the United States in 1954. Its major use is as an herbicide, but its use is now limited to noncrop applications (NCI DCE, 1985i). All registered uses on food crops were cancelled in 1971 (HSDB, 1997).

### **PRODUCTION**

Amitrole does not appear to be presently produced in commercial quantities in the United States (HSDB, 1997), and no suppliers were provided in the *Chemcyclopedia 98* or the 1998 *Chemical Buyers Directory* (Rodnan, 1997; Tilton, 1997). No production data have been reported since the late 1980s (USITC, 1987-1991, 1993-1995). It was produced by one company in 1985 in an undisclosed amount (SRIc, 1985). In 1985, total U.S. imports were 580,000 lb (USDOC Imports, 1986), while in 1982 the figure was 456,000 lb (HSDB, 1997). These volumes are low compared to the 1.2 million lb imported into the United States in 1978 (HSDB, 1997). The 1979 TSCA Inventory identified one company producing 5,500 lb of amitrole and three importers in 1977; no import volumes were reported. The CBI Aggregate was less than 1 million lb (TSCA, 1979).

# **EXPOSURE**

The primary routes of potential human exposure to amitrole are inhalation and dermal contact. For the general population, exposure may occur mainly through ingestion of contaminated food or drinking water or inhalation of contaminated air near areas of high usage, such as herbicidal spraying (HSDB, 1997). No residues of amitrole, however, have been detected in food and water following recommended use (IPCS, 1994a).

Particulates containing amitrole may be released during its production; atmospheric levels ranging up to 100 mg/m<sup>3</sup> and river concentrations from 0.5 to 2 mg/L have been measured near one plant (IPCS, 1994a). After application, amitrole can persist in soil for several weeks and in water for more than 200 days (HSDB, 1997). The potential for exposure to amitrole exists during its manufacture or packaging and during its application as an herbicide. According to NIOSH, about 83 persons were possibly exposed to amitrole during its production, but no data are available on the number of people who potentially are exposed during its application or on the possible exposure levels in the public. The ACGIH recommended a threshold limit value (TLV) of 0.2 mg/m<sup>3</sup> as the time-weighted average (TWA) (ACGIH, 1996).

#### REGULATIONS

EPA regulates amitrole under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) and Resource Conservation and Recovery Act (RCRA). Under RCRA and CERCLA, EPA subjects amitrole to reporting requirements. A reportable quantity (RQ) of 10 lb has been established for the compound. NIOSH recommended a TWA of 0.2 mg/m³ for amitrole (NIOSHc, 1996). OSHA has also specified 0.2 mg/m³ as the permissible exposure limit (PEL). OSHA regulates amitrole under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-9.